PEC 01

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2024-11-03

Contents

PEC 01 · Las ómicas

Abstract

Objetivos

El objetivo del presente informe es investigar la relación entre la pérdida de masa muscular (denominada cachexia) y los datos metabolómicos de un conjunto de muestras biológicas.

Materiales y métodos

Los datos analizados en este estudio fueron obtenidos de esta URL sobre un conjunto de muestras de orina de pacientes diagnosticados con cachexia y controles sanos.

Los datos fueron almacenados para su organización en la clase SummarizedExperiment con la finalidad de integrar los datos y metadatos de las muestras. Adiocionalmente se realizó un analisis de componentes principales (PCA) para analizar las variaciones entre grupos, y determinar los metabolitos específicos que estan asociados a la cachexia.

Resultados

Generación del contendor

Se realiza un análisis del conjunto de datos metabolómicos obtenidos del conjunto de muestras de orina. Comenzamos cargando los datos a partir del archivo CSV, usando la primera fila de nuestros datos como el título de nuestras filas, lo que corresponde con el ID del paciente. Además reestructuramos la variable Muscle.loss en factores, para facilitar el análisis.

```
human_cachexia <- read.csv("human_cachexia.csv", row.names = 1)

human_cachexia$Muscle.loss <- as.factor(human_cachexia$Muscle.loss)
str(human_cachexia)
```

```
## 'data.frame':    77 obs. of  64 variables:
```

```
##  $ Muscle.loss                : Factor w/ 2 levels "cachexic","control": 1 1 1 1 1 1 1 1 1 1 ...
##  $ X1.6.Anhydro.beta.D.glucose: num  40.9 62.2 270.4 154.5 22.2 ...
##  $ X1.Methylnicotinamide      : num  65.4 340.4 64.7 53 73.7 ...
##  $ X2.Aminobutyrate           : num  18.7 24.3 12.2 172.4 15.6 ...
##  $ X2.Hydroxyisobutyrate      : num  26.1 41.7 65.4 74.4 83.9 ...
##  $ X2.Oxoglutarate            : num  71.5 67.4 23.8 1199.9 33.1 ...
##  $ X3.Aminoisobutyrate        : num  1480.3 116.8 14.3 555.6 29.7 ...
##  $ X3.Hydroxybutyrate         : num  56.83 43.82 5.64 175.91 76.71 ...
##  $ X3.Hydroxyisovalerate      : num  10.1 79.8 23.3 25 69.4 ...
##  $ X3.Indoxylsulfate          : num  567 369 665 412 166 ...
##  $ X4.Hydroxyphenylacetate    : num  120.3 432.7 292.9 214.9 97.5 ...
##  $ Acetate                    : num  126.5 212.7 314.2 37.3 407.5 ...
##  $ Acetone                    : num  9.49 11.82 4.44 206.44 44.26 ...
##  $ Adipate                    : num  38.1 327 131.6 144 15 ...
##  $ Alanine                    : num  314 871 464 590 1119 ...
##  $ Asparagine                 : num  159.2 157.6 89.1 273.1 42.5 ...
##  $ Betaine                    : num  110 245 117 279 392 ...
##  $ Carnitine                  : num  265.1 120.3 25 200.3 84.8 ...
##  $ Citrate                    : num  3714 2618 863 13630 854 ...
##  $ Creatine                   : num  196.4 212.7 221.4 85.6 105.6 ...
##  $ Creatinine                 : num  16482 15835 24588 20952 6768 ...
##  $ Dimethylamine              : num  633 608 735 1064 242 ...
##  $ Ethanolamine               : num  645 488 407 821 365 ...
##  $ Formate                    : num  441 252 250 469 114 ...
##  $ Fucose                     : num  337 198 187 407 26 ...
##  $ Fumarate                   : num  7.69 18.92 7.1 96.54 19.69 ...
##  $ Glucose                    : num  395 8691 1353 863 6836 ...
##  $ Glutamine                  : num  871 602 302 1686 433 ...
##  $ Glycine                    : num  2039 1108 620 5064 395 ...
##  $ Glycolate                  : num  685.4 652 141.2 70.8 26.6 ...
##  $ Guanidoacetate             : num  154 110 183 103 53 ...
##  $ Hippurate                  : num  4582 1737 4316 757 1153 ...
##  $ Histidine                  : num  925 846 284 1043 327 ...
##  $ Hypoxanthine               : num  97.5 82.3 114.4 223.6 66.7 ...
##  $ Isoleucine                 : num  5.58 8.17 9.3 37.71 40.04 ...
##  $ Lactate                    : num  107 369 750 369 3641 ...
##  $ Leucine                    : num  42.1 77.5 31.5 103.5 101.5 ...
##  $ Lysine                     : num  146.9 284.3 97.5 290 122.7 ...
##  $ Methylamine                : num  52.5 23.6 18.7 48.9 27.9 ...
##  $ Methylguanidine            : num  9.97 7.69 4.66 141.17 5.31 ...
##  $ N.N.Dimethylglycine        : num  23.3 87.4 24.5 40 46.1 ...
##  $ O.Acetylcarnitine          : num  52.98 50.4 5.58 254.68 45.6 ...
##  $ Pantothenate               : num  25.8 186.8 145.5 42.5 74.4 ...
##  $ Pyroglutamate              : num  437 437 713 567 185 ...
##  $ Pyruvate                   : num  21.1 37 29.4 64.1 12.3 ...
##  $ Quinolinate                : num  165.7 73 192.5 86.5 38.1 ...
##  $ Serine                     : num  284 392 296 1249 206 ...
##  $ Succinate                  : num  154.5 244.7 142.6 144 68.7 ...
##  $ Sucrose                    : num  45.1 459.4 160.8 111 75.2 ...
##  $ Tartrate                   : num  97.51 32.79 16.28 837.15 4.53 ...
##  $ Taurine                    : num  1920 1261 4273 1525 469 ...
##  $ Threonine                  : num  184.9 198.3 110 376.1 64.1 ...
##  $ Trigonelline               : num  943.9 208.5 192.5 992.3 86.5 ...
##  $ Trimethylamine.N.oxide     : num  2122 639 1153 1451 172 ...
```

```
##  $ Tryptophan                : num  259.8 83.1 82.3 235.1 103.5 ...
##  $ Tyrosine                  : num  290 167.3 60.3 323.8 142.6 ...
##  $ Uracil                    : num  111 47 31.5 30.6 44.3 ...
##  $ Valine                    : num  86.5 110 59.1 102.5 160.8 ...
##  $ Xylose                    : num  72.2 192.5 2164.6 125.2 186.8 ...
##  $ cis.Aconitate             : num  237 334 330 1863 101 ...
##  $ myo.Inositol              : num  135.6 376.1 86.5 247.2 750 ...
##  $ trans.Aconitate           : num  51.9 217 58.6 75.9 98.5 ...
##  $ pi.Methylhistidine        : num  157.6 308 145.5 249.6 84.8 ...
##  $ tau.Methylhistidine       : num  160.8 130.3 83.9 254.7 79.8 ...
```

El siguiente paso fue estructurar los datos para introducirlos en nuestro contenedor. Se crea la matriz de conteo con todos los datos metabolómicos, el objeto colData que contendrá la información de las muestras. Además de el metadata con la información del experimento. Generamos finalmente el objeto SummarizedExperiment con toda la información del experimento.

```
counts <- as.matrix(human_cachexia[, -1])
counts <- t(counts)
colData <- DataFrame(Muscle.loss = human_cachexia$Muscle.loss)

metadata <- list(
  general_information = "Successfully passed sanity check!",
  samples = "Samples are not paired.",
  groups = "2 groups were detected in samples.",
  data_values = "All data values are numeric.",
  missing_values = "A total of 0 (0%) missing values were detected."
)

se <- SummarizedExperiment(assays=list(counts=counts), colData=colData,
                           metadata = metadata)
se
```

```
## class: SummarizedExperiment
## dim: 63 77
## metadata(5): general_information samples groups data_values
##   missing_values
## assays(1): counts
## rownames(63): X1.6.Anhydro.beta.D.glucose X1.Methylnicotinamide ...
##   pi.Methylhistidine tau.Methylhistidine
## rowData names(0):
## colnames(77): PIF_178 PIF_087 ... NETL_003_V1 NETL_003_V2
## colData names(1): Muscle.loss
```

```
dimnames(se)
```

```
## [[1]]
##  [1] "X1.6.Anhydro.beta.D.glucose" "X1.Methylnicotinamide"
##  [3] "X2.Aminobutyrate"            "X2.Hydroxyisobutyrate"
##  [5] "X2.Oxoglutarate"             "X3.Aminoisobutyrate"
##  [7] "X3.Hydroxybutyrate"          "X3.Hydroxyisovalerate"
##  [9] "X3.Indoxylsulfate"           "X4.Hydroxyphenylacetate"
## [11] "Acetate"                     "Acetone"
## [13] "Adipate"                     "Alanine"
## [15] "Asparagine"                  "Betaine"
## [17] "Carnitine"                   "Citrate"
## [19] "Creatine"                    "Creatinine"
```

```
## [21] "Dimethylamine"               "Ethanolamine"
## [23] "Formate"                     "Fucose"
## [25] "Fumarate"                    "Glucose"
## [27] "Glutamine"                   "Glycine"
## [29] "Glycolate"                   "Guanidoacetate"
## [31] "Hippurate"                   "Histidine"
## [33] "Hypoxanthine"                "Isoleucine"
## [35] "Lactate"                     "Leucine"
## [37] "Lysine"                      "Methylamine"
## [39] "Methylguanidine"             "N.N.Dimethylglycine"
## [41] "O.Acetylcarnitine"           "Pantothenate"
## [43] "Pyroglutamate"               "Pyruvate"
## [45] "Quinolinate"                 "Serine"
## [47] "Succinate"                   "Sucrose"
## [49] "Tartrate"                    "Taurine"
## [51] "Threonine"                   "Trigonelline"
## [53] "Trimethylamine.N.oxide"      "Tryptophan"
## [55] "Tyrosine"                    "Uracil"
## [57] "Valine"                      "Xylose"
## [59] "cis.Aconitate"               "myo.Inositol"
## [61] "trans.Aconitate"             "pi.Methylhistidine"
## [63] "tau.Methylhistidine"
##
## [[2]]
##  [1] "PIF_178"      "PIF_087"      "PIF_090"      "NETL_005_V1"  "PIF_115"
##  [6] "PIF_110"      "NETL_019_V1"  "NETCR_014_V1" "NETCR_014_V2" "PIF_154"
## [11] "NETL_022_V1"  "NETL_022_V2"  "NETL_008_V1"  "PIF_146"      "PIF_119"
## [16] "PIF_099"      "PIF_162"      "PIF_160"      "PIF_113"      "PIF_143"
## [21] "NETCR_007_V1" "NETCR_007_V2" "PIF_137"      "PIF_100"      "NETL_004_V1"
## [26] "PIF_094"      "PIF_132"      "PIF_163"      "NETCR_003_V1" "NETL_028_V1"
## [31] "NETL_028_V2"  "NETCR_013_V1" "NETL_020_V1"  "NETL_020_V2"  "PIF_192"
## [36] "NETCR_012_V1" "NETCR_012_V2" "PIF_089"      "NETCR_002_V1" "PIF_179"
## [41] "PIF_114"      "NETCR_006_V1" "PIF_141"      "NETCR_025_V1" "NETCR_025_V2"
## [46] "NETCR_016_V1" "PIF_116"      "PIF_191"      "PIF_164"      "NETL_013_V1"
## [51] "PIF_188"      "PIF_195"      "NETCR_015_V1" "PIF_102"      "NETL_010_V1"
## [56] "NETL_010_V2"  "NETL_001_V1"  "NETCR_015_V2" "NETCR_005_V1" "PIF_111"
## [61] "PIF_171"      "NETCR_008_V1" "NETCR_008_V2" "NETL_017_V1"  "NETL_017_V2"
## [66] "NETL_002_V1"  "NETL_002_V2"  "PIF_190"      "NETCR_009_V1" "NETCR_009_V2"
## [71] "NETL_007_V1"  "PIF_112"      "NETCR_019_V2" "NETL_012_V1"  "NETL_012_V2"
## [76] "NETL_003_V1"  "NETL_003_V2"
```

```
colData(se)
```

```
## DataFrame with 77 rows and 1 column
##              Muscle.loss
##                 <factor>
## PIF_178         cachexic
## PIF_087         cachexic
## PIF_090         cachexic
## NETL_005_V1     cachexic
## PIF_115         cachexic
## ...                  ...
## NETCR_019_V2     control
## NETL_012_V1      control
## NETL_012_V2      control
```

```
## NETL_003_V1      control
## NETL_003_V2      control
```

A partir de nuestro objeto **se** podemos obtener la matriz de conteos con las concentraciones de los metabolitos para cada muestra. Además podemos filtrar los datos de metabolitos por grupo de muestras así como ver las distribuciones de las medias entre los mismos.

```
counts <- assay(se)
head(counts,3)
```

```
##                              PIF_178 PIF_087 PIF_090 NETL_005_V1 PIF_115 PIF_110
## X1.6.Anhydro.beta.D.glucose   40.85   62.18  270.43      154.47   22.20  212.72
## X1.Methylnicotinamide         65.37  340.36   64.72       52.98   73.70   31.82
## X2.Aminobutyrate              18.73   24.29   12.18      172.43   15.64   18.36
##                              NETL_019_V1 NETCR_014_V1 NETCR_014_V2 PIF_154
## X1.6.Anhydro.beta.D.glucose      151.41        31.50        51.42  117.92
## X1.Methylnicotinamide             36.60         6.82        30.27   52.46
## X2.Aminobutyrate                   8.67         4.18         7.54   19.49
##                              NETL_022_V1 NETL_022_V2 NETL_008_V1 PIF_146 PIF_119
## X1.6.Anhydro.beta.D.glucose       20.70      127.74       59.74   89.12   23.57
## X1.Methylnicotinamide            221.41      177.68       50.91   32.79    6.89
## X2.Aminobutyrate                  15.18       12.68        6.82   10.38    2.12
##                              PIF_099 PIF_162 PIF_160 PIF_113 PIF_143
## X1.6.Anhydro.beta.D.glucose   41.26  589.93  112.17  167.34  183.09
## X1.Methylnicotinamide          8.67   21.98   25.28   19.89   90.92
## X2.Aminobutyrate               2.56   15.18   15.49   13.46    8.94
##                              NETCR_007_V1 NETCR_007_V2 PIF_137 PIF_100
## X1.6.Anhydro.beta.D.glucose       208.51        34.81  333.62   32.46
## X1.Methylnicotinamide              53.52        95.58   35.87    9.68
## X2.Aminobutyrate                    5.26        23.57    7.92    3.90
##                              NETL_004_V1 PIF_094 PIF_132 PIF_163 NETCR_003_V1
## X1.6.Anhydro.beta.D.glucose        4.71   68.72  214.86  304.90        37.71
## X1.Methylnicotinamide             11.13   13.87  127.74   25.79        10.80
## X2.Aminobutyrate                  43.38   12.18   31.50   27.11         5.00
##                              NETL_028_V1 NETL_028_V2 NETCR_013_V1 NETL_020_V1
## X1.6.Anhydro.beta.D.glucose       45.60       34.12       107.77       13.33
## X1.Methylnicotinamide            473.43       92.76        16.61       50.91
## X2.Aminobutyrate                  16.28        8.25        26.84        2.92
##                              NETL_020_V2 PIF_192 NETCR_012_V1 NETCR_012_V2
## X1.6.Anhydro.beta.D.glucose       27.94  141.17        14.01       244.69
## X1.Methylnicotinamide             80.64   68.03        46.06       116.75
## X2.Aminobutyrate                  15.80   40.85        29.08        40.04
##                              PIF_089 NETCR_002_V1 PIF_179 PIF_114 NETCR_006_V1
## X1.6.Anhydro.beta.D.glucose  123.97       141.17   35.16  685.40       278.66
## X1.Methylnicotinamide         81.45        28.50   26.58   36.23        40.45
## X2.Aminobutyrate              55.15        20.29    5.21   32.46        55.15
##                              PIF_141 NETCR_025_V1 NETCR_025_V2 NETCR_016_V1
## X1.6.Anhydro.beta.D.glucose   15.80        29.96        16.95       292.95
## X1.Methylnicotinamide         23.57        96.54       114.43        57.97
## X2.Aminobutyrate              17.99         6.55         2.53       167.34
##                              PIF_116 PIF_191 PIF_164 NETL_013_V1 PIF_188 PIF_195
## X1.6.Anhydro.beta.D.glucose   29.67   18.92  127.74       34.81   65.37   15.18
## X1.Methylnicotinamide         70.11   24.53 1032.77       12.30   24.05   94.63
## X2.Aminobutyrate               5.58    3.29    8.58        5.87    4.71   11.36
##                              NETCR_015_V1 PIF_102 NETL_010_V1 NETL_010_V2
```

```
## X1.6.Anhydro.beta.D.glucose        70.81   25.28       34.47       18.54
## X1.Methylnicotinamide              75.94  101.49       12.81        8.41
## X2.Aminobutyrate                   22.65    8.33        3.78        3.78
##                             NETL_001_V1 NETCR_015_V2 NETCR_005_V1 PIF_111
## X1.6.Anhydro.beta.D.glucose       37.34        33.78        22.42  146.94
## X1.Methylnicotinamide             55.15        53.52        55.15   10.07
## X2.Aminobutyrate                   7.39        18.17        20.70    6.30
##                             PIF_171 NETCR_008_V1 NETCR_008_V2 NETL_017_V1
## X1.6.Anhydro.beta.D.glucose   64.07        32.46       113.30       22.20
## X1.Methylnicotinamide          6.42        14.01        43.38       20.70
## X2.Aminobutyrate              28.79         2.97         4.66        7.85
##                             NETL_017_V2 NETL_002_V1 NETL_002_V2 PIF_190
## X1.6.Anhydro.beta.D.glucose       46.53      192.48      528.48   28.79
## X1.Methylnicotinamide              9.78      108.85      225.88    9.21
## X2.Aminobutyrate                   3.10        7.77       13.46    5.53
##                             NETCR_009_V1 NETCR_009_V2 NETL_007_V1 PIF_112
## X1.6.Anhydro.beta.D.glucose      181.27        47.47       15.96   22.87
## X1.Methylnicotinamide             48.42         7.69       16.12   10.38
## X2.Aminobutyrate                   8.94         4.06        1.93    1.28
##                             NETCR_019_V2 NETL_012_V1 NETL_012_V2 NETL_003_V1
## X1.6.Anhydro.beta.D.glucose       35.16       16.95        9.39       37.71
## X1.Methylnicotinamide             52.46       15.80       14.01       18.17
## X2.Aminobutyrate                  13.87       10.49        5.16       26.05
##                             NETL_003_V2
## X1.6.Anhydro.beta.D.glucose       38.47
## X1.Methylnicotinamide             12.55
## X2.Aminobutyrate                  15.03
```

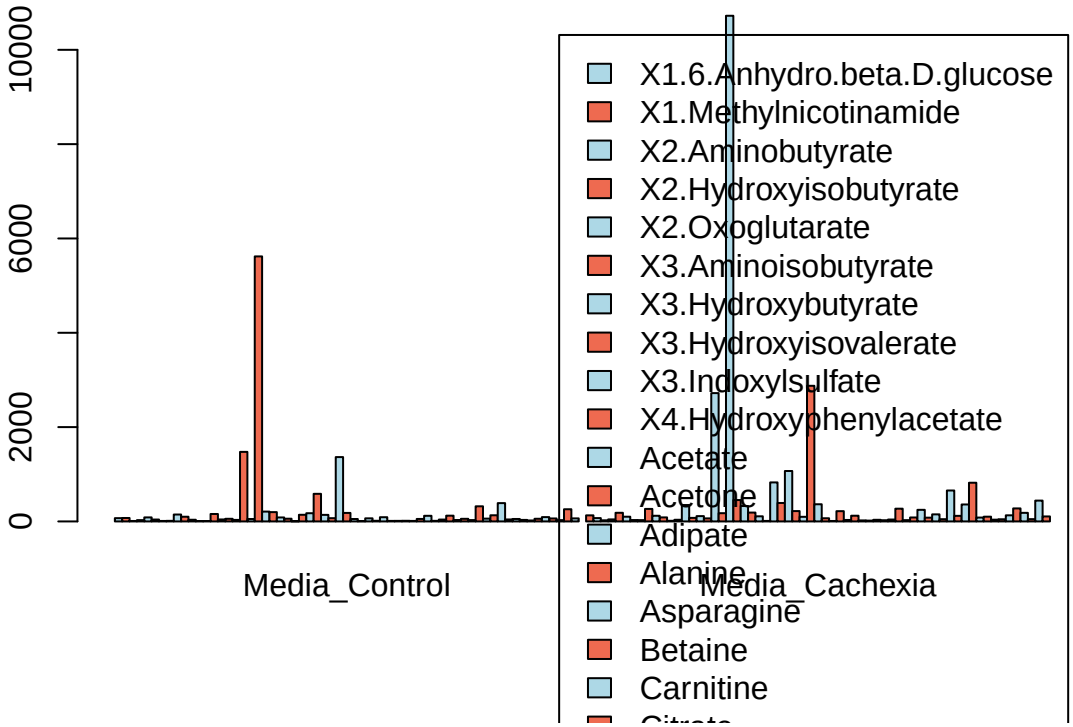
```
mean_control <- rowMeans(counts[,se$Muscle.loss=="control"])
mean_cachexia <- rowMeans(counts[,se$Muscle.loss=="cachexic"])

mean_comparison <- data.frame(
  Media_Control = mean_control,
  Media_Cachexia = mean_cachexia
)
mean_comparison
```

```
##                             Media_Control Media_Cachexia
## X1.6.Anhydro.beta.D.glucose     69.505333     128.688936
## X1.Methylnicotinamide           73.155000      70.564255
## X2.Aminobutyrate                 9.528333      23.669149
## X2.Hydroxyisobutyrate           27.871000      43.237660
## X2.Oxoglutarate                 85.517333     183.110426
## X3.Aminoisobutyrate             39.911000     100.274681
## X3.Hydroxybutyrate               9.898667      29.260638
## X3.Hydroxyisovalerate           12.312667      27.606383
## X3.Indoxylsulfate              146.376333     265.157660
## X4.Hydroxyphenylacetate         99.798667     119.822553
## Acetate                         35.604667      85.632979
## Acetone                          8.420000      13.346383
## Adipate                          8.993333      34.817872
## Alanine                        157.584000     347.591064
## Asparagine                      41.749000      75.390851
## Betaine                         55.970333     112.252979
## Carnitine                       32.443667      64.622128
```

```
## Citrate                       1474.718667    2720.852766
## Creatine                        51.504333     174.913404
## Creatinine                    5619.174667   10722.140213
## Dimethylamine                  208.683333     453.580638
## Ethanolamine                   197.125333     326.772128
## Formate                         84.483333     187.564468
## Fucose                          57.444667     108.599149
## Fumarate                         4.552000      10.921915
## Glucose                        140.958000     827.218936
## Glutamine                      174.427333     391.410426
## Glycine                        585.149333    1069.377872
## Glycolate                      138.983667     219.269574
## Guanidoacetate                  68.739667      97.624255
## Hippurate                     1364.240333    2875.729574
## Histidine                      180.472333     364.232340
## Hypoxanthine                    51.714333      67.087021
## Isoleucine                       7.218000       9.660851
## Lactate                         65.748333     217.631915
## Leucine                         13.556667      31.261702
## Lysine                          89.229333     121.282340
## Methylamine                     11.360000      21.216383
## Methylguanidine                 12.128333      17.364681
## N.N.Dimethylglycine             13.596667      34.489787
## O.Acetylcarnitine               10.598000      25.564468
## Pantothenate                    52.622667      39.944043
## Pyroglutamate                  119.258000     270.292340
## Pyruvate                        12.566333      26.865532
## Quinolinate                     39.324000      83.747234
## Serine                         122.263000     245.829787
## Succinate                       29.836000      79.628936
## Sucrose                         55.579667     150.024468
## Tartrate                        28.676000      47.234681
## Taurine                        320.522333     655.720000
## Threonine                       59.518667     118.233191
## Trigonelline                   130.687000     359.637660
## Trimethylamine.N.oxide         388.669000     820.340638
## Tryptophan                      41.833000      81.824043
## Tyrosine                        52.014000     100.742340
## Uracil                          32.493333      37.513617
## Valine                          20.132667      45.582553
## Xylose                          56.509333     129.289149
## cis.Aconitate                   91.724000     276.025532
## myo.Inositol                    62.641333     181.837660
## trans.Aconitate                 27.809333      48.814043
## pi.Methylhistidine             258.640000     441.553191
## tau.Methylhistidine             64.650333     105.667660
```

```r
barplot(as.matrix(mean_comparison),
        beside = TRUE,
        col= c("lightblue", "coral2"),
        legend = rownames(mean_comparison))
```



Exploración de datos

Discusión y conclusiones

Repositorio de Github